

KEYES (E. L.)  
THE

# TREATMENT OF SYPHILIS,

WITH

SPECIAL REFERENCE TO THE CONSTITUTIONAL REMEDIES  
APPROPRIATE TO ITS VARIOUS STAGES,

THE DURATION OF THEIR USE, AND THE QUESTION OF  
THEIR CONTINUOUS OR INTERMITTENT  
EMPLOYMENT.

BY

EDWARD L. KEYES, M.D.,

PROFESSOR OF DERMATOLOGY IN THE BELLEVUE HOSPITAL MEDICAL COLLEGE, NEW YORK.

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EXTRACTED FROM THE TRANSACTIONS OF THE  
INTERNATIONAL MEDICAL CONGRESS,  
PHILADELPHIA, SEPTEMBER, 1876.

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## THE TREATMENT OF SYPHILIS.

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- I. Does a mild beginning in syphilis necessarily indicate that the malady will run a mild course, so that the duration of treatment may be regulated thereby?
- II. Is the internal use of mercury debilitating?
- III. When is mercury useful in syphilis? Has it any control over the late symptoms?
- IV. When is iodine useful in syphilis? Can it replace mercury in any stage of the disease?
- V. Does iodine act by liberating mercury lying latent in the tissues?
- VI. Should treatment be continuous or interrupted?
- VII. General outline of a course of internal treatment.
- VIII. Conclusions, negative and positive.

I. *Does a mild beginning in syphilis necessarily indicate that the malady will run a mild course so that the duration of treatment may be regulated thereby?*—My subject restricts me to the constitutional remedies appropriate to the different stages of syphilis, and I shall keep as closely within the prescribed limits as the nature of the question will allow. It is necessary, however, to answer this first proposition before taking up the general consideration of constitutional treatment.

I need not cite authorities to prove that syphilis, commencing mildly, is often looked upon as a trivial, self-limited disease. Such a belief prevails in the minds of many physicians to-day. It has received the sanction of high authority. Diday,<sup>1</sup> of Lyons, has taught it boldly for many years, and Lancereaux in the main supports his views. Diday divides syphilitic patients into two classes. Of these, one class, embracing about two-thirds of the whole number, says Diday,<sup>2</sup> contains cases beginning mildly. The prognosis in these cases is declared to be good; the patients are treated mainly by expectation; and mercury is considered unnecessary and even harmful. Cases commencing severely, the other class, get mercury; but, so the teaching goes, they only get it as an evil less bad than the severe syphilis which it is used to counteract, and the obvious conclusion is that the remedy must be employed during only a short time to overcome the symptoms, and must not be continued to

<sup>1</sup> Histoire naturelle de la Syphilis; Paris, 1863.

<sup>2</sup> Diday et Doyon, Thérapeutique des Maladies vénériennes et des Maladies cutanées; Paris, 1876, p. 254.

the injury of the patient. *Lancereaux*<sup>1</sup> is particularly strong on this point, and I think that a similar conviction is widespread among the profession in this country, the general notion being that mercury is bad, and only to be used because syphilis is worse. And even if this were not so, and if the profession should become a unit in regarding any given case of syphilis as liable to prove serious in the end, yet it would still be impossible to subject all cases commencing lightly to prolonged treatment. The ordinary patient can neither convince himself, nor be convinced—after his first alarm is over, and his trivial early eruption past—that he is likely to suffer severely from his disease at some indefinite, future period, and in the conviction that he will not so suffer, his physician is very apt to encourage him.

It is certainly true that most cases of syphilis commencing mildly continue to preserve their mild type whether treated or not, and are not so apt to lead to serious later troubles as where the earlier lesions are bad, the chancre, perhaps, phagedenic, and the first eruption pustular. It is natural that this should be so. Phagedæna is a personal peculiarity, and not a syphilitic symptom, and it is fair to assume that the quality of constitution which allows phagedæna to occur in a given chancre, will also cause the symptoms which follow it to be proportionally severe. It is the same with a tendency to form pus on light provocation, either in the elimination of an internal poison, or from external cause; this pyogenic tendency is a personal matter and by no means a symptom of syphilis, and where it shows itself in the early outbreaks of the disease by a pustular or even by a vesicular eruption, it is only natural that the course of the future symptoms should prove severe.

That these qualities of phagedæna, pustulation, etc., are personal, and not due to the acquisition of any especially bad type of disease, I think is easily demonstrable. I have seen more than once two patients whose syphilis had been derived from the same source, run a widely different course in their symptoms. The fact seems to me to be that an individual shows himself up physically when he is prostrated by the first onset of syphilis. A light beginning in the disease seems to indicate that the patient has power to rally and make a good fight. The physician, therefore, lulls himself into a belief that the patient can manage his disease without much aid from medicine, and, as the remedy, mercury, is regarded as an evil, he concludes that the patient is best off with as little of it as possible.

This reasoning would be unimpeachable were the premises accurate, but they are not so. First, mercury is not an evil. It is not debilitating, but tonic, in health as well as in disease, when continuously used in minute doses. This I think can be proved, and, if so, it becomes obvious that even if only a small percentage of the mild cases of syphilis become severe after a lapse of years, it is justifiable to submit all cases to such a continuous treatment as, itself tonic and beneficial to the patient, shall prove capable of keeping down symptoms during its use and for a considerable period afterward. Second, no one can tell how many cases commencing mildly may become severe in the end. That very many do

<sup>1</sup> *Traité de la Syphilis*; Paris, 1874, p. 548. "Un certain nombre de spécialistes, etc. . . se croient obligés d'administrer le mercure pendant plusieurs mois, quelquefois même pendant des années; . . . loin de s'opposer à la marche ultérieure de la maladie, ils conduisent le malade à l'anémie ou à l'obésité."



change in type is certain. The journals abound in such cases, and the experience of those who are accustomed to deal with the disease is always rich in incidents bearing on this point. I need not go beyond my own note-book to illustrate this.

CASE I.<sup>1</sup>—A gentleman had chancre and a faint eruption for which he took mercury in considerable doses during a few months. After ten years of health, he had syphilitic iritis, and a gummy destructive ulcer on the penis which resisted eight weeks of energetic treatment (caustics, etc.) at the hands of a surgeon, and cicatrized in three weeks under steadily increasing doses of the iodide of potassium.

CASE II.<sup>2</sup>—A medical student had chancre and indurated inguinal glands which were unmistakably syphilitic. He underwent treatment by small doses of mercury at my hands. His type of disease was so mild that he had no eruption whatever, nor any sign or symptom of disease except one indolent, indurated, post-cervical ganglion. Therefore he concluded that I was in error, and stopped his treatment entirely after a few months. In eighteen months I treated him for syphilitic hemiplegia. He had had no symptom meanwhile.

CASE III.—A physician got an insignificant sore, followed by a slight papular rash. He took no mercury, but was treated by cathartics. The rash went away, and he remained perfectly well for nine years. Then a lump appeared upon the top of his head, and remained stationary during eleven years. But now the patient had a fever, and, on getting up from it, the node spread, softened, and swept away an enormous piece of his skullcap. The wound healed kindly under the use of iodide of potassium.

CASE IV.<sup>3</sup>—A gentleman had urethral chancre. No eruption followed that he could remember. He certainly took no mercury, and remained well for twelve years, when he broke out with syphilitic ecthyma which disappeared after the use of arsenic for a time. Then his brain gave out, and was declared to be softening by one of the most noted experts in nervous disease in Europe. Finally this got better spontaneously, and a rapidly advancing, gummy, destructive ulceration invaded his soft palate. This got well immediately, with great improvement in his other symptoms, under the use of iodide of potassium alone.

CASE V.—A physician got chancre. A few mucous patches in the mouth followed, but, he stated, no eruption whatever. He took mercury for a year. Not a symptom appeared for thirty years. Then he died during a sharp attack of intellimental and convulsive troubles which he would not treat, not believing them to be syphilitic. The autopsy revealed a large gummy tumor in his brain.

CASE VI.—A gentleman got chancre followed by a light eruption. This was treated homœopathically and disappeared. Sixteen years afterwards he applied for treatment, being almost covered with nodes. He had ulcers in his throat and syphilitic lung disease. Steady improvement attended the mixed treatment.

CASE VII.—A gentleman got chancre and fell into the hands of an anti-mercurialist who dosed him freely and continuously for a year with iodide of potassium and sarsaparilla. His earlier symptoms were not severe. In one year ulcers appeared on both legs. The dose of the iodide was increased. The ulcers progressed in depth and area, three on the right leg measuring over one inch in diameter each. He now changed his physician. His new adviser discontinued the iodide of potassium and ordered protiodide of mercury. Improvement began at once. In two weeks the ulcers were cicatrized. He now ceased treatment, but, after two years, a gummy ulcer destroyed a portion of the septum of the nose; for this he consulted me.

<sup>1</sup> Van Buren and Keyes, *Genito-Urinary Diseases*, etc.; New York, 1874, p. 537.

<sup>2</sup> *Ibid.*, p. 650.

<sup>3</sup> Van Buren and Keyes, *Clinical Contribution*, etc., *Archives of Dermatology*, vol. i. p. 108. Cases III. IV. V. and VI. were seen by me in connection with Dr. Van Buren.



These cases are not very exceptional. The list could be largely increased, but I restrict myself to these few cases because they sustain the point at issue from almost every side, and because some of them bear also upon other facts which will be used in subsequent portions of this paper. It will be seen that all these cases had a very light syphilitic attack in the beginning, and that they were all managed differently. Case I. had a light eruption, and took mercury in considerable doses for a few months. Case II. had no early eruption, and took a very little mercury for a very short time. Case III. took no mercury, but was treated by cathartics. Case IV. took no mercury, but was treated by balsams, because his chancre was urethral, and his malady mistaken for gonorrhœa. Case V. took mercury for one year, and remained well for thirty. Case VI. was treated homœopathically. Case VII. was treated for one year with iodide of potassium. I have had no patient who had been syphilized, but the seven cases cover nearly all the other methods of treatment: that by expectation; by cathartics; by diuretics (balsam, etc.); by mercury for a short time in large doses, for a short time in small doses, for a year in fair doses; by homœopathy; by iodide of potassium from the first—and all of these, starting mildly, turned out to be severe cases of syphilis.

It is indeed notorious how many bad cases of disease there are in which there has been very little early eruptive trouble, and in which the previous history of the patient shows treatment only during a few months. This treatment for a few months seems to be what nearly all cases get, and although very many of them, be they light or severe at first, escape serious subsequent trouble, yet there is no guarantee in the prevailing modes of treatment that they will so escape, *nor can a light beginning be counted upon to signify a type of disease necessarily mild.*

I have not thought it necessary to search among the array of corroborative cases which modern journals afford for material to further substantiate this point, preferring to adhere to personal cases, for the history of which I can vouch. I cannot, however, refrain from alluding to a recent article by Fournier,<sup>1</sup> a record of forty-seven cases of cerebral syphilis, and itself a strong argument against the too readily accepted maxim that mild syphilis needs but little treatment. Of the forty-seven cases only two were severe from the first, one was rather bad, thirty were ordinary cases, and fourteen “actually benign.” One of these latter was the case of a medical student who got what is termed “un chancre de rien” (a mere trifle of a chancre), had a little papular rash and sore throat only, and took mercury for a few months. After seventeen years of calm, there came an explosion of syphilitic epilepsy, hemiplegia, hebetude, dementia, and death in spite of all the skill and care of Fournier and Ricord. My conclusions to this introductory section therefore are: (1) that all syphilis is severe and treacherous, and that further efforts are justifiable in attempting to perfect its treatment; and (2) that seemingly light cases need as thorough a course of medication as those cases which are apparently more severe.

II. *Is the internal use of mercury necessarily debilitating?*—Time would fail me should I attempt to go into this question exhaustively, yet upon its solution hangs the strongest possible argument for or against a con-

<sup>1</sup> La Syphilis cérébrale, est elle plus commune dans certaines formes de la diathèse, etc., L'École de Méd., Aug. 30, 1875.



tinuous use of mercury. If mercury is an evil, if its influence is debilitating, then its use would only be justified by its ability to overcome some greater evil, some more debilitating agent; and it should be dispensed with in every case as quickly as possible. This indeed is the accepted view of the mercurial question in syphilis. I think, however, that it may be shown: (1) That mercury in minute doses is a tonic, and, (2) That mercury in minute doses has been in use in the profession as a tonic, in non-syphilitic cases, for very many years, and sanctioned by the highest authority.

(1) That mercury in minute doses increases the number of the red blood cells both in syphilitic and in healthy individuals, I think I have demonstrated with the *hématomètre*, publishing my results in the January (1876) number of the *American Journal of the Medical Sciences*. To that paper I must refer for details. Space will not allow me to reproduce the evidence here. I have, however, corroborated the conclusions therein reached by repeated, new experiments, during the present year, and these conclusions I beg leave to adduce in evidence now. They are based upon the counting of red blood-corpuscles in over one hundred different specimens of blood, which number has been greatly added to since the publication of the paper without occasioning any modification in the results at first arrived at. These conclusions are: (a) That 5,000,000 red corpuscles in the cubic millimetre of blood is a full, high average for the adult, healthy male, etc. (in New York); (b) That mercury decreases the number of the red cells when given in excess, especially in hospitals (this was also conclusively proved by Wilbouchewitch<sup>1</sup>); (c) That syphilis diminishes the number of red corpuscles below the healthy standard; (d) That mercury in small doses, continued for a short or for a long period, in syphilis, alone or with the iodide of potassium, increases the number of red corpuscles in the blood, and maintains a high standard of the same; (e) That mercury in small doses acts as a tonic upon healthy animals, increasing their weight. (Liegeois and Bennett cited.) In larger doses it is debilitating or fatal; (f) That mercury in small doses is a tonic<sup>2</sup> to individuals in fair health, not syphilitic. In such individuals it increases the number of the red blood-corpuscles.

I must again express regret that I cannot bring out the evidence here, which led directly up to these conclusions in such a way that I can see no possible escape from them, and, referring those interested to the original paper, I again ask to incorporate these conclusions as a part of my present argument. This proof of the tonic action of minute doses of mercury is scientific, but the demonstration from the *clinical side* is no less positive.

(2) We are all familiar with the well-known tonic consisting of a minute dose of corrosive sublimate in compound tincture of bark. I first learned it from the late Valentine Mott, who was loud in its praises as an "alterative" in the cases of strumous children. I cannot trace the authorship of this compound. It is very favorably mentioned as having "been long recommended both for scrofulous taint and the more declared forms of tuberculosis," in Copland's *Dictionary of Practical Medicine*, 1858;<sup>3</sup> and I find it spoken of as a preparation in common use, in a

<sup>1</sup> De l'influence des Préparations mercurielles sur la Richesse du Sang en Globules rouges et en Globules blancs. *Archives de Physiologie*, 4 et 5, 1876, p. 508.

<sup>2</sup> During as long a period as the experiments were kept up. Keyes, loc. cit.

<sup>3</sup> Vol. iii. p. 760.



lecture by Sir Astley Cooper, which appeared in the *Lancet* in 1823.<sup>1</sup> He praises it as an alterative "for the removal of chronic diseases in children." Modern ideas of "alterative action" are not very clear, and in connection with this mixture I never understood how mercury could be beneficial, until the truth flashed upon me, while counting blood corpuscles with the *hématimètre*, that mercury in minute doses was tonic in all cases in which it could be digested. I think that this tonic action of mercury in small doses must have had much to do with establishing the professional confidence in former days in so-called alterative<sup>2</sup> medication.

This conviction of the value of minute doses of mercury as an "alterative" (*i. e.*, tonic), not in syphilis but in all chronic disease, I find to be most deeply rooted in the minds of the older members of our profession throughout the country. I have received many letters, from far and near, from representative men, stating that they had inherited the faith from their preceptors, and had been for years in the habit of using minute doses of mercury, long-continued, as an alterative in chronic debilitating disease; that they had used it empirically, but with good effect. I have received similar answers from all the older men whom I have questioned. What can be stronger evidence than this that mercury in minute doses is tonic, increasing the vitality of the individual; and when to this is added the scientific proof, by actual counting, that mercury increases the number of the red blood-corpuscles, the chain of evidence seems complete. It may be well here to mention a remedy on which many of the profession in New York were accustomed to rely some years ago with confidence for the cure (or certainly the relief) of Bright's disease. It was two grains of corrosive sublimate in an ounce of tincture of the sesquichloride of iron. The dose was ten drops (not minims), containing about one-fiftieth of a grain of bichloride of mercury, a very fair tonic dose; and that improvement attended its use in many cases, is unquestionable. Finally may be cited the popular sanction of minute doses of mercury as a tonic which is found in the history of Swaim's Panacea,<sup>3</sup> a nostrum at one time in very general use. This remedy consisted of a minute quantity of corrosive sublimate in compound syrup of sarsaparilla. Swaim is believed to have gotten the idea from an old book, his first business having been that of a book binder.

While then all the evidence goes to show that minute doses of mercury are tonic, out of syphilis as well as in it, the proof is equally strong that mercury in large doses is debilitating, if at all continued, whether in syphilis or out of it. This is proved by history, by clinical experience, and by actual blood counting with the *hématimètre*, as has been shown by Wilbouchewitch and by myself, in the articles already referred to.

<sup>1</sup> Vol. i. p. 111.

<sup>2</sup> J. Kent Spender, of London, refers to the action of corrosive sublimate (*Journal of Cutaneous Medicine*, No. 15, 1870, p. 187), saying that it indirectly promotes the nutrition of several tissue elements, and speaks of Dr. Billing's mention of its action as tonic. In a letter to me, Dr. Spender says that Billing (*First Principles of Medicine*, 5th ed. 1849, p. 109) states that the "tonic" action of mercury illustrates the rationale of the operation empirically called "alterative." He does not enlarge or explain further.

<sup>3</sup> Dr. E. R. Squibb, of Brooklyn, informs me that this nostrum, appearing about the year 1825, was extensively advertised, and enjoyed unbounded popularity, bringing great wealth to its inventor. In 1828, Prof. Hare, of the University of Pennsylvania, discovered mercury in the mixture. He published the fact in the *Amer. Journ. of Med. Sciences*, vol. iv., 1829, p. 530, whereupon Swaim denied that the "Panacea" contained mercury. In fact mercury does not *now* seem to be one of the ingredients. Mr. Neergaard analyzed a specimen of Panacea for me, but failed to find any mercury.



III.—*When is mercury useful in syphilis? Has it any contro<sup>l</sup> over the late symptoms?*—If it be once admitted that mercury is useful during any stage of syphilis, the proof that it is a tonic theoretically establishes its value during all stages of the disease; for the hématinètre on the one hand, and clinical observation on the other, prove conclusively that syphilis is essentially a debilitating malady, and that it lessens the number of the red blood-cells. Yet mercury is not alone tonic, it is antidotal to syphilis; not only generally to syphilitic symptoms, but specifically when locally applied, as Koebner<sup>1</sup> has shown, particularly for condylomata, referring also to Ch. Hunter and Hebra; and as Monti<sup>2</sup> has demonstrated by causing the local disappearance of patches of eruption by injecting the bichloride subcutaneously into them, while other patches at a distance remained comparatively unaltered. In a general syphilitic eruption, the advantage of combining local with general means is strikingly shown by the much more prompt disappearance of lesions which have been subjected to the local use of mercury, than of the same lesions elsewhere seated and not locally treated. This I have repeatedly noticed.

Every one admits the power of mercury in postponing and modifying the earlier symptoms of syphilis, and of shortening their course when they do appear. Even the anti-mercurialists allow this, their claim being either that mercury prolongs the attack on the whole by postponing the symptoms, since the disease must run its course—or that it suppresses the virus and causes the appearance of tertiary lesions by debilitating the constitution, or in some other way. No statistical or other evidence with which I am familiar has ever established either of these assumptions,<sup>3</sup> while the almost universal advocacy of mercury in syphilis, in one form or another, by a majority of the best minds in the profession in all countries, goes far to show that this is the only honest remedy for syphilis with which the profession is familiar. As for the two points of the anti-mercurialists—that mercury used early only postpones the symptoms, prolonging the total duration of the disease, and that tertiary symptoms are due to mercury—if time allowed, any number of cases might be cited in opposition to this view; such as Cases III. and IV. of this paper, in which, no mercury having been used, the disease was in full force after twenty-one and fifteen years respectively, in the most advanced tertiary type; or Case VII., in which mercury cured

<sup>1</sup> Archiv f. Derm. u. Syph., B. L., S. 628; quoted from Jahresber. d. schles. Gesellsch. f. vaterländ. Cultur.

<sup>2</sup> Jahrbuch. f. Kinderheilkunde, 1869, S. 381. Beobachtung über die Behandlung der Syphilis congenita et acquisita mittelst subcutaner sublimatinjectionen.

<sup>3</sup> Undoubtedly statistics exist on both sides of the question, but they fail to prove anything positive. Quite recently Jullien (Gaz. Hebdom., Sept. 18 and Oct. 2, 1874), in a statistical paper attempting to establish the proportion of cases of tertiary disease occurring in those who had taken mercury for their earlier symptoms, as compared with those who had been otherwise treated, found in 218 cases of tertiary disease that 59, more than one quarter, had not taken mercury, while all the rest had taken it. The number of cases of nervous syphilis he noted to be much greater proportionally in those who had taken mercury. All this, however, proves nothing except that syphilis naturally runs on to tertiary symptoms when untreated. Statistics cleverly handled are capable of proving almost any thing in relation to syphilis, because the disease itself is so capricious. In this case the statistics were made up from letters received from physicians in France, England, and Italy, and undoubtedly in these countries three-quarters of the well known physicians give mercury early in syphilis, and it would be but fair that three-quarters of the cases of tertiary syphilis found should turn out to have taken this remedy. This is especially probable when the statistics are compiled by one who is no lover of the drug, and his figures lose all value when it is remembered that there is no record of the cases which did not become tertiary under the mercurial and anti-mercurial courses.

tertiary ulcers, which failed to improve under fair doses of iodide of potassium, in a patient who had been treated by the latter remedy alone for a year after his chancre appeared.

That mercury retains its value late in syphilis is amply illustrated by the well-recognized power of the mercurial, general fumigation, in many advanced forms of syphilitic ulceration, late in the disease; by the great value of what is known as the mixed treatment, especially in controlling peculiarly chronic and grave symptoms of late syphilis; and by the numerous cases of nervous syphilis found in the journals of the day, in which the turn in the symptoms is noted as the point at which the gums became touched. Occasionally a case is found in which the customary forms of iodine cannot be borne late in syphilis, or in which they do not seem to meet the requirements of the disease. Under these circumstances an appeal to mercury alone will often yield a victory over symptoms until then rebellious. Case VII. of this paper is in point, mercury having succeeded where iodine had failed. While then it seems not doubtful that mercury retains its power in every stage of syphilis, yet it is no less true that it cannot be relied upon in emergencies in certain, especially the gummy, forms of tertiary disease. Here the different preparations of iodine take the lead.

As a final illustration of the power of mercury over tertiary lesions may be cited its undoubted value in inherited syphilis. Here the lesions are grouped in a disorderly manner—tertiary, perhaps gummatous, disease of the bones, lungs, kidney, thymus gland and liver, often accompanying secondary symptoms on the skin and mucous membranes—yet in these cases mercury is generally relied upon, and often proves capable alone of routing the enemy. I conclude, therefore, that mercury is of value during the whole treatment of syphilis, in minute doses throughout, for its tonic and anti-syphilitic action; in larger doses, as the occasion arises, to suppress outcropping symptoms, the action here being purely anti-syphilitic, and not tonic.

IV. *When is iodine useful in syphilis? Can it replace mercury in any stage of the disease?*—In studying this point, I have again had recourse to the *hémاتمètre* to watch the effect upon the red blood-corpuscles of the internal administration of the preparations of iodine. My conclusion, based upon a considerable number of blood-counts made by myself, and many by my friend Dr. L. A. Stimson, is that iodide of potassium is a tonic, and increases the number of the red blood-cells. It does this in all stages of syphilis. I have not yet tried its effect upon the healthy individual, but notably in some experiments by Dr. Stimson this point came out, that while iodide of potassium, given immediately after the appearance of a chancre, increased the red blood-cells with proportionally greater rapidity than did mercury given under similar conditions (for the effect of mercury during the first depression preceding the outcrop of the earliest eruption is often very slight), yet, in spite of this greater increase in the number of the red blood-cells, the administration of iodide of potassium did not retard the appearance of the secondary symptoms to the same extent as did the use of mercury. This fact corresponds to the well-known results of the experiments of Grassi, who determined that iodide of potassium increased, while mercury decreased, the proportion of the red blood-cells to the whole mass of blood when used in syphilis. In Grassi's day, mercury, when used at all, was



always given in excess, and his conclusions, although obtained by chemical methods mainly, are undoubtedly accurate.

These statements of Grassi have been made use of to construct a rule of practice; namely, to give iodides and tonics early in syphilis, avoiding the supposed depressing influence of mercury. But when it appears that the iodides do not seriously interfere with the outcrop of the early eruptions, while mercury certainly does; and when it turns out that mercury in small doses (but large enough to greatly modify the disease) is tonic, the rule of practice founded on Grassi's experiments fails to find any scientific support, and must fall to the ground. Case VII. in this paper illustrates this point. This patient was dosed with iodide of potassium for a year, but his early eruptions appeared none the less, although they were undoubtedly mild, and his tertiary symptoms came on in due time, perhaps as early as they would have come had no treatment been used. Iodine doubtless has some modifying influence over syphilis during its whole course, but not enough to make it wise to substitute this drug for its more powerful rival early in the disease.

I see no reason to believe that iodine has any eliminative power in syphilis, and I have failed to discover any evidence to show that it tends to prevent relapse. That it holds a place, however, in the treatment of syphilis, is undoubted; and a very high place it is. When tissue-infiltrations take place; when the lesion approaches the gummatous type; when there is considerable connective-tissue proliferation, especially if it takes place rapidly, whether the affection is of an external or of an internal organ; when nodes form upon the bones; when the cartilages begin to soften; when ulceration is spreading rapidly, then the preparations of iodine used unsparingly for the symptom are the right hand of treatment. Here nothing can replace iodine. To its benign influence, when well assimilated and rapidly pushed, the most formidable lesions yield a quick response.

In certain of the chronic lesions occurring late in syphilis, the power of mercury is greatly enhanced by combining some preparation of iodine with it; but where the lesion is a gumma, mercury may be dispensed with at once, and entirely, and iodine pushed with a lavish hand until the symptom yields. Mercury, however, must be resumed to seal the cure and prevent relapse, and it must be given with long patience and scrupulous care that it is thoroughly assimilated. In syphilis, therefore, when the lesion is gummatous, no matter where it is situated, iodine may replace mercury with profit to the patient; but under no other circumstances can it take the place of this drug, although it may often be advantageously combined with it. Iodine is indeed what many have considered mercury to be, a remedy not at all curative of syphilis, but causing the disappearance of certain of its symptoms. A curative agent it is not, because it has little if any power of shortening the duration of the disease, of keeping off or modifying many of its symptoms, or of preventing relapse.

V. *Does iodine act by liberating mercury lying latent in the tissues?*—I think that this question may be briefly disposed of in the negative. That iodine taken at the same time renders a given quantity of mercury more active, is probable, this being perhaps the secret of the success of the mixed treatment for chronic obstinate lesions, not gummatous. But whatever power as an anti-syphilitic remedy iodine possesses, it probably exercises by its merit as a tonic, increasing the number of red cells in

the blood; for this it does even early in the disease, in spite of the depressing influence of the virus.

When a patient has been carrying a certain amount of mercury without showing it in the mouth, the sudden administration of iodide of potassium may call forth symptoms of salivation. Indeed, iodides given alone, in some exceptional cases, have produced quite marked symptoms of mild salivation. But a little positive evidence outweighs any amount of negative testimony, and whatever power iodine may have in rendering mercury active, still, in its own sphere, in controlling gummy exudation in any of its forms, iodine does not yield a hair's breadth to any remedy, or demand the least assistance from mercury. An excellent case bearing on this point was printed editorially in the *Gazette des Hôpitaux* for January 28, 1860.<sup>1</sup> Cases III. and IV. of this paper are directly in point, iodine alone having cured patients who had never taken mercury. Case VII. might be referred to as evidence on the other side; but, as I have already stated, some forms of tertiary disease, notably some of the ulcers, seem to demand mercury for their treatment, and yield to it much more promptly than to iodine. In this case, also, I could not ascertain to what extent the iodide had been pushed, and at best the evidence is negative, while the other is positive.

The late Prof. Boeck, of Christiania, informed me, while in this country, that, when tertiary symptoms occurred in his patients who had been treated solely by syphilization, he was in the habit of using iodide of potassium with good effect, combined with a continuance of syphilization. In these cases surely there was no antecedent mercury, the liberation of which could do the work. And finally, in proof that the iodine possesses the power, it is only necessary to recall that, in those frightful cases of devastating disease which we sometimes meet with, and which yield to the iodides, the dose must not be restricted, but pushed with rapidity up to the point of tolerance, the amount of the dose assimilated being in direct relation to the rapidity of cure.

VI. *Should treatment be continuous or interrupted?*—The answer to this question has already been brought out in what has been written. The continuous use of iodine need hardly be considered, for I feel unable to include this drug among the curative agents of syphilis. It has enormous power in overcoming certain symptoms, but as these symptoms are intermittent, the use of iodine should also be interrupted. While the symptom lasts, and for a certain time afterwards, iodine is called for; but as it does not prevent relapse, or shorten the whole course of the disease, there is no occasion for its prolonged use. Mercury, on the other hand, has received the palm as the anti-syphilitic, at least the symptomatic, anti-syphilitic, remedy, *par excellence*, from a majority of the best medical scholars and authorities up to the present time. It is an antidote to the poison, whatever the nature of that poison may be. I think that the results of blood-counting by the *hématinètre*, used upon the blood of syphilitic patients who had taken small doses of mercury continuously for long periods (over three years),<sup>2</sup> proves that mercury is not debilitating, but, indeed, a tonic, when used in minute doses.

<sup>1</sup> Although the writer states that he thinks iodine often does not act well unless mercury has been previously used.

<sup>2</sup> Keyes, *loc. cit.*



Clinical experience also has convinced me of the value of the continued treatment. I have employed it in all cases, light or severe, in which I could control the patient, since the early spring of 1869. Generally I have not commenced treatment until the post-cervical and epitrochlear, glandular engorgement, and an eruption, have come to confirm the diagnosis. My observation has included nearly all the cases of my partner, Professor Van Buren, and I have to thank him for his kindly suggestions which have led to many of the steps in this investigation, an investigation which has convinced us both more than ever of the value of the uninterrupted use of mercury in small doses in the treatment of syphilis. It has become a rule with us, to which we find but few exceptions, that patients, after acquiring syphilis, remain in as good and often in better health while under treatment than previously. Severe cases are the rarest of exceptions, and tertiary symptoms (in those treated from the start) nearly unknown. Slight localized lesions, such as a scaly spot on the palm, a cluster of a few papules here or there, appearing from time to time, are, customarily, all that mark a continuance of the disease, except the lesions of the throat and mouth. Slight ulcers about the throat, mucous and scaly patches in the mouth and on the tongue, are apt to persist and recur at intervals, for long periods. These are the main, very often the only, symptoms requiring attention after the first eruption has passed, and they respond to local measures, or to a slight increase in the strength of the general treatment.

Usually the continuous treatment is kept up for from two and a half to three and a half years, or even longer, and in all cases, if possible, until six months, and sometimes a year or more, after the appearance of the last syphilitic symptom. Many of the patients so treated are now married and raising healthy families—themselves to all appearances perfectly well.

Of course it is impossible to state how many of these patients are absolutely exempt from any further relapse. Seven years and a half are not sufficient to pass final judgment on any method, but against other methods may be urged: (1) That the numerous bad cases constantly met with have all been treated by them; (2) That salivation is certainly harmful; (3) That mercury, not pushed to salivation, but used in large doses, has been proved to be debilitating by the *hématinètre* (Wilbouchewitch, Keyes), by clinical experience, and by experiments upon animals (Liegeois, Bennett, Wilbouchewitch, and others); (4) That the intermitting treatment is simply symptomatic, and virtually makes one confess that he has no remedy for the disease, but can only moderate the symptoms until such time as they may see fit to cease to reappear.

For the continued treatment with minute doses of mercury it may be urged, on the other hand: (1) That it has given good results thus far (seven and a half years); (2) That it is scientifically and theoretically correct to use continuously for a given evil an antidote which can itself be proved to be beneficial to the individual, be he sick or well; (3) That it seems proper to use an antidote continuously against a poison which is continuous, although having long periods of latency. For the poison must be continuous and still present in the tertiary stage, although it has then lost much of its virulence and power of transmissibility. How else can we account for the undoubted fact that parents with tertiary disease may produce children with inherited syphilis (I have notes of such cases), and inherited syphilis is well known to be capable of transmitting itself in full force to the nurse and other healthy persons by contact; (4)

That this continued treatment is only a modification of the "coup sur coup" plan, so widely practised, for the quantity of mercury is augmented upon any outcrop of symptoms, the minute, continuous dose being maintained in the intervals. It is, indeed, not very widely different from the common, symptomatic, interrupted treatment, yet I cannot but believe that it is a great improvement upon both of the ordinary plans.

VII. *General outline of a course of treatment in a typical case.*—When the first eruption appears, or sooner if by confrontation or other sure means the existence of syphilis is placed beyond any possible doubt, my habit has been to put the patient upon a mercurial, and to increase the dose, slowly if there is time, more rapidly if the eruption is pressing, paying all possible attention to hygiene, food, surroundings, care of teeth, etc., until slight diarrhœa with colicky pain is complained of, or until the gums just begin to be touched. The amount required to produce this effect is now known to be the patient's dose, beyond which he cannot safely go without aid from opiates, or changing the form of administering the drug, and at which, if it is maintained, the effect on the general health will be injurious. Having found this dose, it may be maintained, if the eruption demands it, by giving opium, bismuth, rice, milk, etc., until the symptom yields; then it should be reduced to one half, or a little below this point (this dose will prove tonic to the patient), and there maintained day after day, continuously, year in and year out, waiting for other symptoms.

Should such symptoms occur, for there may be none except mucous patches, which local means will relieve, I think it is well to give the patient mercurial baths,<sup>1</sup> when practicable, two or three times a week or oftener if they do not prove depressing, maintaining the same internal dose. Instead of this, the half dose held in reserve may be immediately or gradually added to the tonic dose, or inunction may be practised, until the symptoms are subdued, when the tonic dose is to be again resumed and unremittingly continued.

Later in the disease, should any of those symptoms supervene which are known to be favorably influenced by iodine, the iodide of potassium or sodium may be combined with the mercurial (preferably with the biniodide of mercury), and the two continued (mixed treatment).

Should cerebral symptoms come on; or bones, or nerves, or muscles, or viscera, or any of the tissues become involved in any of the forms of gummatous growth (this, however, I have not yet seen in any case where the directions have been strictly followed from the first); then the iodides are to be used unsparingly for the symptom, it being of little importance whether the mild mercurial is continued for the time being or not.

Many deviations from this simple course may be necessitated by varying cases, especially when the continuous treatment is only commenced late in the disease. I think that a case treated from the first symptom should receive mercury continuously, in small doses, for a period not less than two and a half years, or, in any event, until at least six months have passed after the entire disappearance of the last clearly syphilitic symptoms. It is hardly necessary to add that all treatment may be sus-

<sup>1</sup> Two drachms of black oxide after a few minutes of steam (not hot air), the whole bath to last not over twenty minutes, is a fair average.



pended without ultimate disadvantage should any acute disease accidentally occur within the limits of this time.

My time has expired, and it would be hopeless for me to attempt to take up a consideration of exceptional cases, either of patients such as those who cannot take mercury or iodine, or of peculiar forms of disease, or surrounding circumstances, where these remedies seem powerless, and where an appeal to change of air, or to derivation by the bowels (Zittman's decoction), or derivation by the skin (syphilization or tartarization), seems to effect more than can be done by following the rules established by success in the majority of cases.

I cannot consider the value of mercury locally, as a means of treatment of the lesions, or of other local remedies; nor the relative value of iodine used as the tincture (internally), or as the iodide of potassium, of sodium, of ammonium, of calcium, or of amylum, or as metallic iodine with albumen, or as iodoform; nor of the varied use of these agents by the stomach or rectum. My remarks have been general, and intended to apply to the typical case, and I have endeavored to group them so as to lead up to the following negative and positive conclusions, which I now beg respectfully to lay before you, and on which I ask the expression of your opinion.

*Negative Conclusions.*—Views for which there would seem to be no positive foundation in fact:—

- I. Syphilis commencing mildly needs but little treatment, and does not require mercury.
- II. Mercury given internally is necessarily debilitating.
- III. Mercury is only useful in secondary syphilis.
- IV. Iodide of potassium is of considerable value in secondary syphilis.
- V. Iodide of potassium is of no value unless preceded by the use of mercury.
- VI. Iodide of potassium acts by liberating mercury which has been lying latent.

*Positive Conclusions.*—Propositions which, in the present state of our knowledge, may be affirmed:—

- I. Mercury is an antidote to the syphilitic poison, and of service in controlling all its symptoms in all (even the latest) stages of the disease, its power over gummata being least marked, and not to be relied upon.
- II. Mercury in minute doses is a tonic.
- III. Iodine cures certain symptoms of syphilis, but does not prevent relapse.
- IV. The use of mercury, long-continued, uninterruptedly as far as practicable, in small doses, from the time of the earliest eruption, constitutes the best treatment of syphilis.







